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Hierarchical Bayes models for Perfusion Imaging

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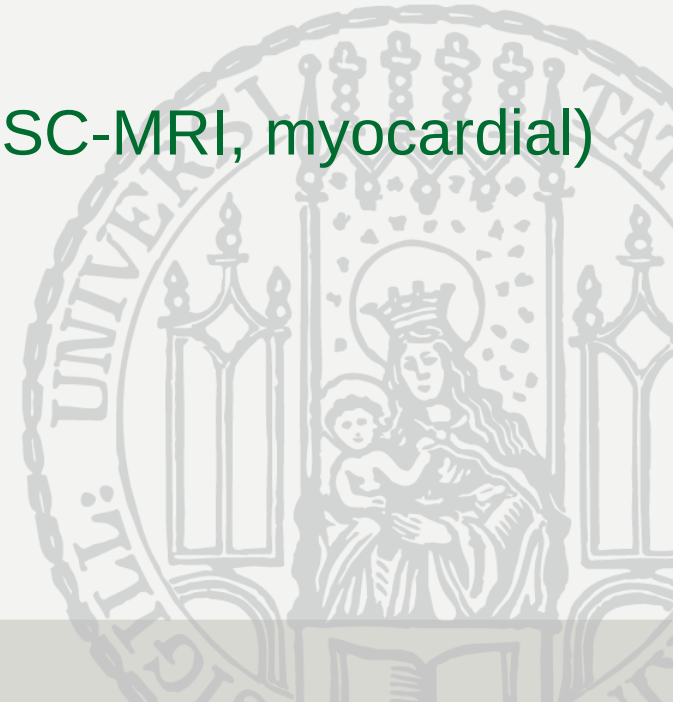
Perfusion Imaging

Interest in imaging blood perfusion *in vivo*

Detection and quantification of areas with pathological high or low blood flow

Applications:

- Oncology (DCE-MRI)
- Ischemic diseases (strokes, DSC-MRI, myocardial)
- Rheumatology



Contrast-Enhanced MRI

MRI allows non-invasive in-vivo imaging

Imaging of magnetic properties

→ use magnetic contrast agent (CA)

CA travels via blood stream, allows to assess perfusion into tissue

E.g. in oncology (DCE-MRI):

- Angiogenesis: Growth of vessels from cancerous tissue
- Detection/Size measurement
- Diagnostics
- Evaluation of therapy

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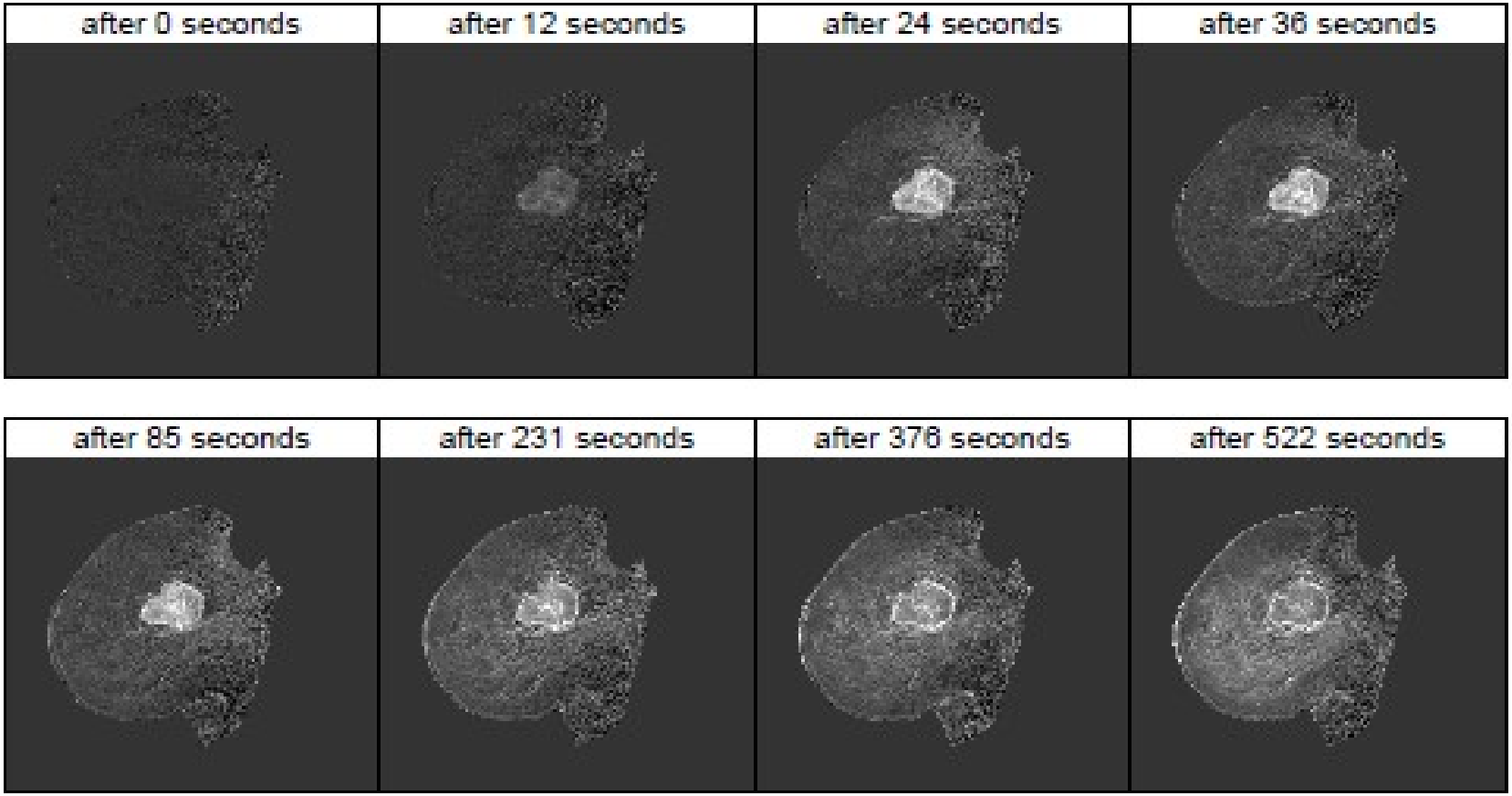
DCE-MRI - Data



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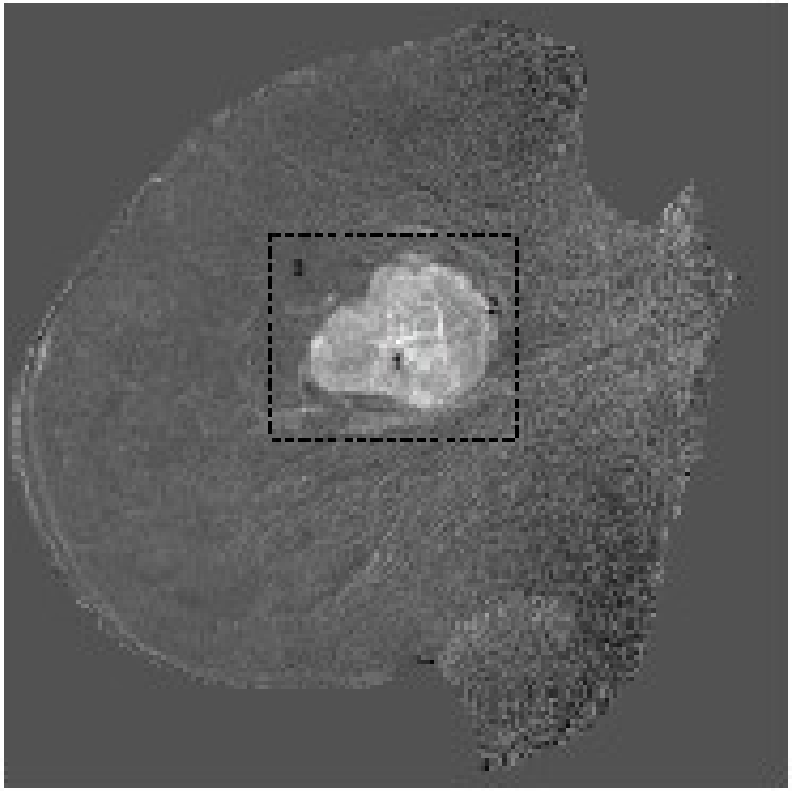
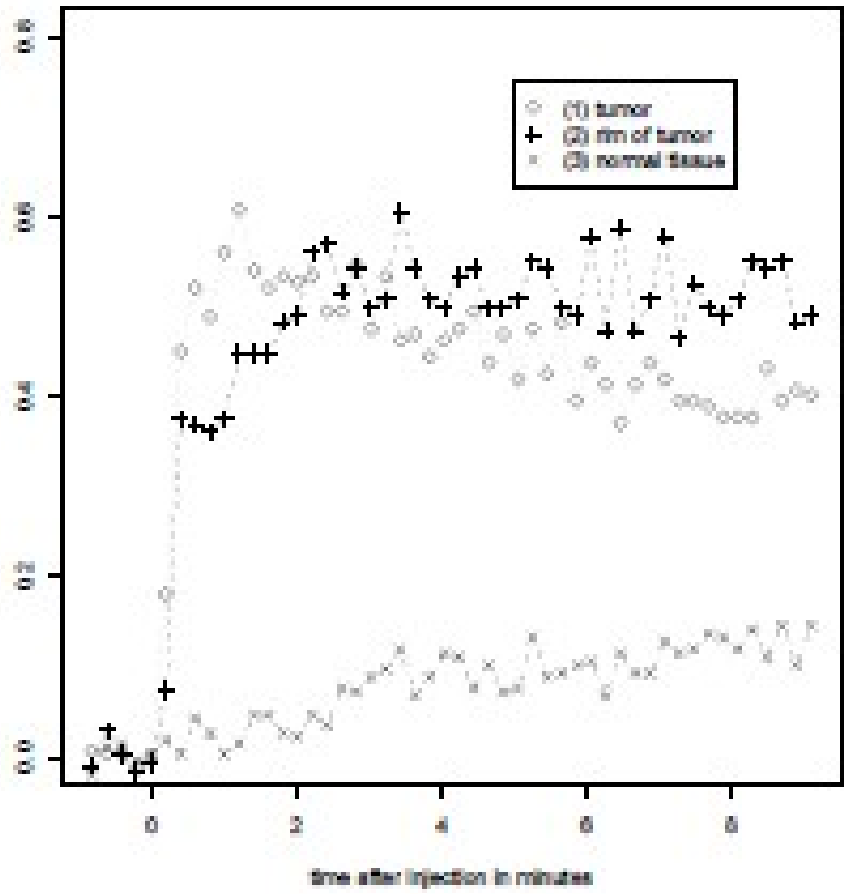
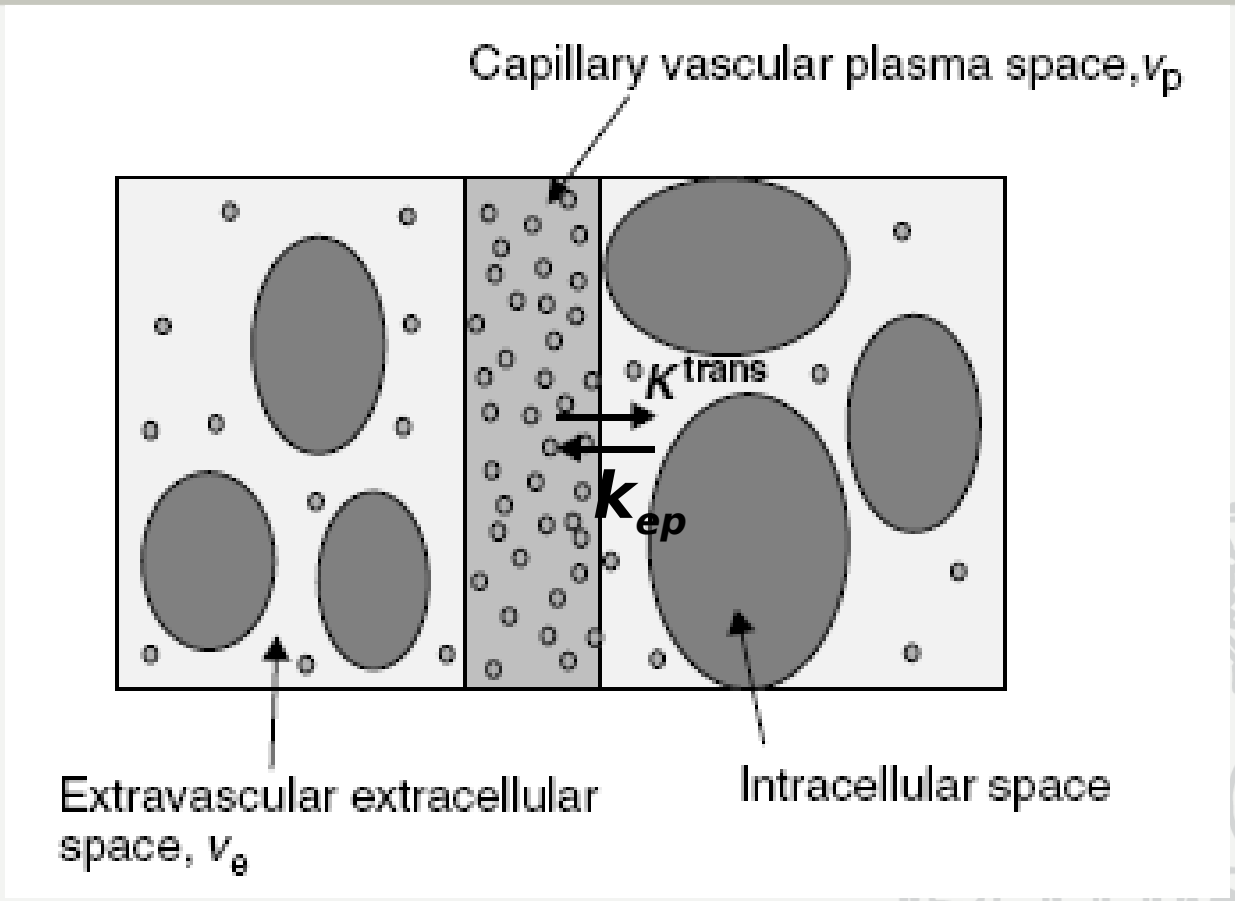
DCE-MRI - data





Compartment Model for DCE-MRI



$$C_t(t) = v_p C_p(t) + K^{trans} \int_0^t C_p(u) \exp(-k_{ep}(t-u))\, du$$

Myocardial Perfusion

$$S(t) = A(t) \otimes f(t)$$

A(t) measured in left ventricle blood pool

$$S = \mathbf{A}f = \mathbf{A}\mathbf{B}\beta = D\beta$$

Jerosch-Herold et al. (IEEE TMI 2004)

Response *f* modeled as penalized B-Spline

$$f(t) = \sum_{p=1}^{P} B_{pt}\beta_p \qquad \beta_{ip} \sim \mathbf{N}(\beta_{i,p-1}, \lambda^2)$$

Schmid (IEEE TMI 2011)

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Other local models

- Linear Models → fMRI (e.g., Brezger, Fahrmeir, Hennerfeind 2009 JRSS)
- Two-, N-compartment models
  - Model choice
  - See Kaercher, Schmid, ISBI 2010)
- Stochastic differential equations (for FRAP)
  - See Dargatz, 2010

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Non-linear Regression

- Model for breast cancer

$$C_t(t) = DK^{trans} \sum_{i=1}^{2} \frac{a_i \left(\exp(-m_i t) - \exp(k_{ep} t) \right)}{k_{ep} - m_i}$$

- AIF parameters D, a_1, a_2, m_1, m_2 known
- Least square algorithm (Levenberg-Marquardt)
  - Starting values?
  - Convergence?
  - Biological not realistic values ($K^{trans} > 20$)

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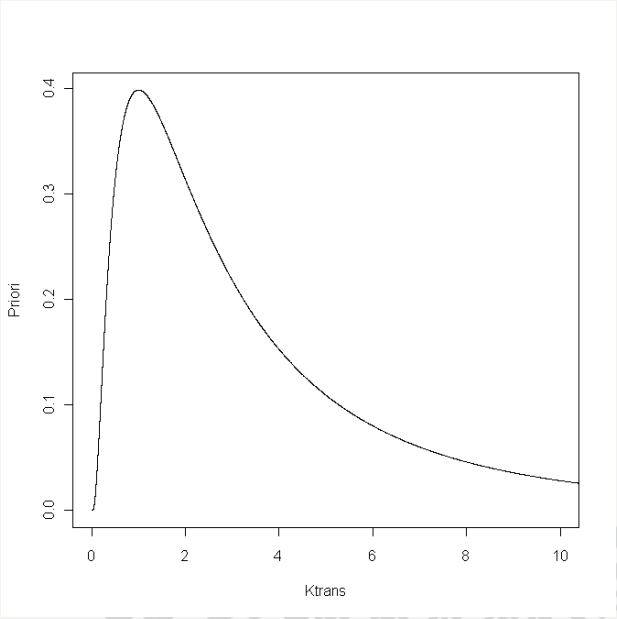
Bayes Approach

Use Priori-Information:

$$\theta = \log(K^{trans}) \sim N(0,1)$$

$$\phi = \log(k_{ep}) \sim N(0,1)$$



$$p(K^{trans},k_{ep}|Y) = \frac{l(Y)\, p(K^{trans},k_{ep})}{\int l(y)\, p(h)\, dh}$$

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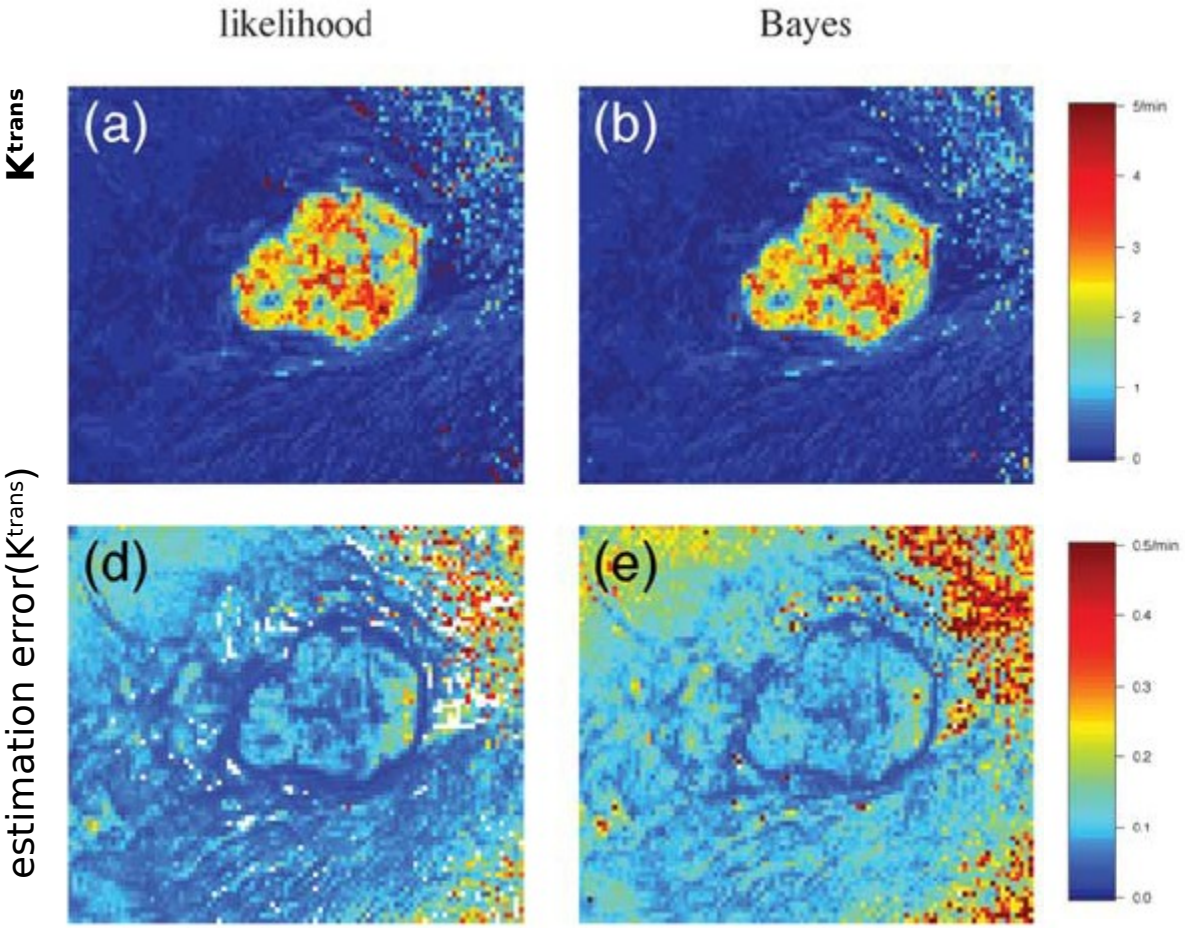
Parameter maps



Schmid, Whitcher, Padhani, Taylor, Yang, IEEE TMI (2006), 25:12, 1627-1636

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Contextual information

- Although models are simplified, model fitting is typically challenging
  - "Very non-linear"
  - Low signal-to-noise ratio
  - Convolution

→ Use contextual information to make model fitting more robust ("borrowing strength")

- Use contextual model to test dependencies

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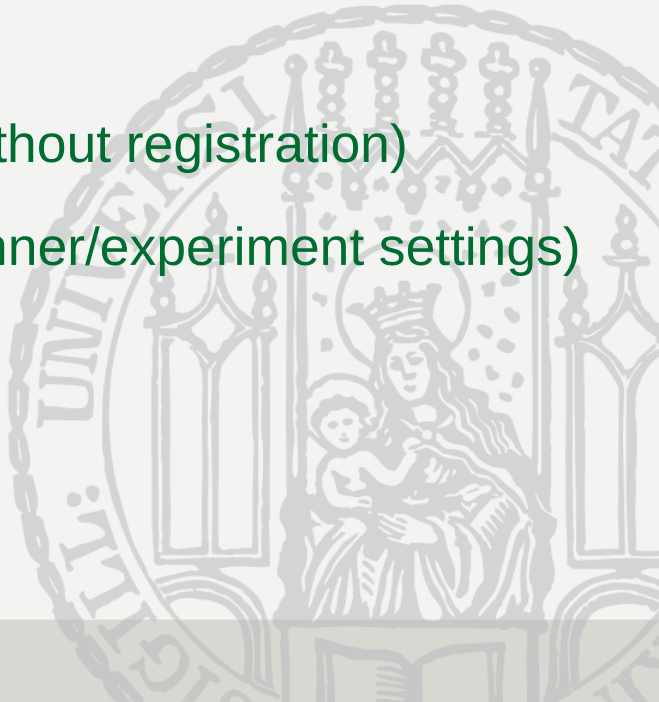
Contextual information

- Spatial information, inherent in images
  - Adjacent voxels share same tissue, have similar properties
  - Voxel grid is arbitrary
  - But: account for edges, sharp features
- Meta information
  - Images from same object (with or without registration)
  - Covariates (patient information, scanner/experiment settings)
  - Additional observations (e.g. EEG)



Hierarchical Modelling

Level 1: Noise structure

Level 2: Local model (Cinetics)

Level 3: Contextual information (e.g., spatial)

Level 4: Hyper parameters (e.g., smoothing parameters)

- Prior information on latent, unobserved parameters
- “Flat priors”

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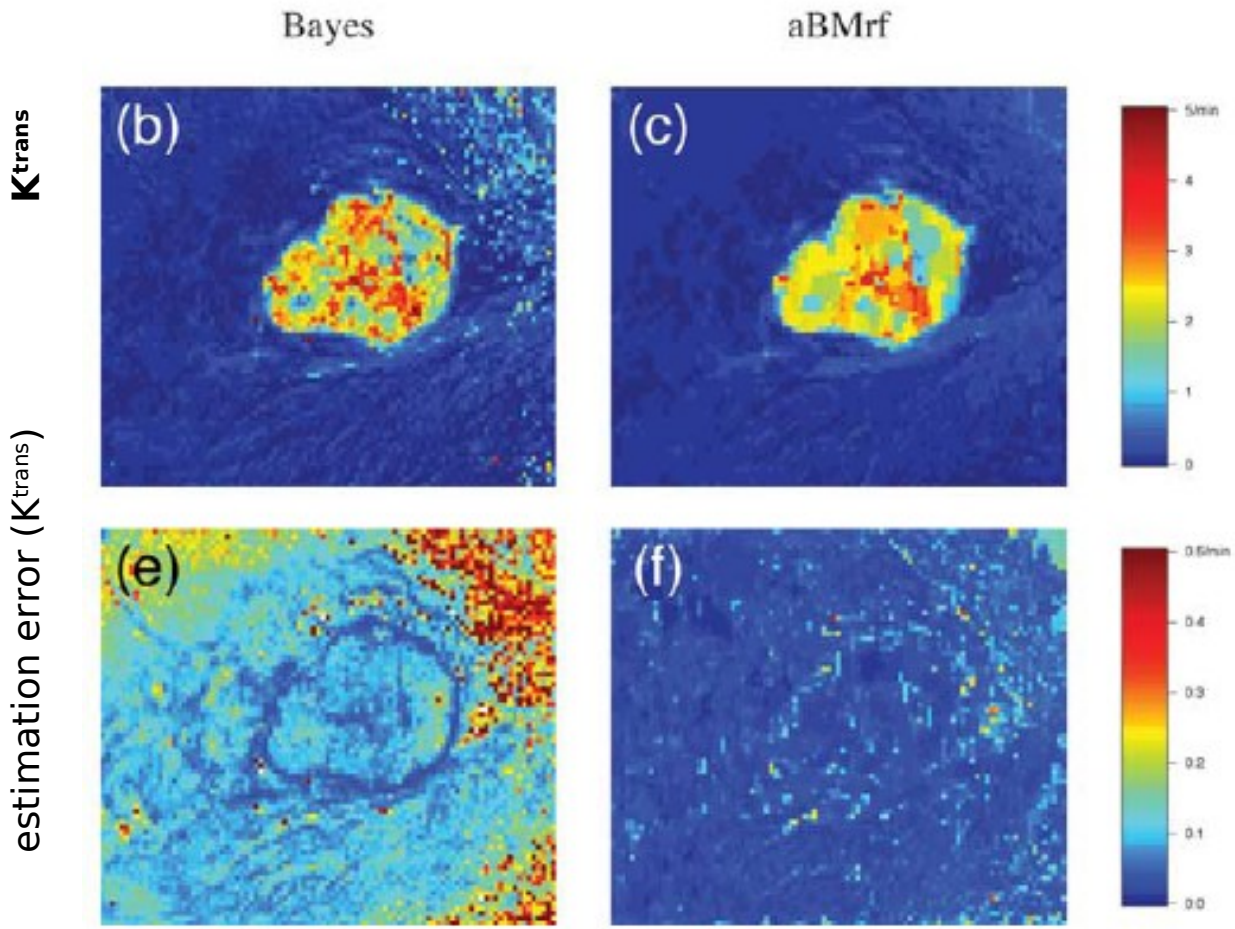
Markov random field for DCE-MRI

- Assumption: Adjacent voxel have similar kinetic parameters
- Markov random field on K^{trans} and k_{ep}

$$\log\left(K_i^{trans}\right) \sim \mathrm{N}\left(\sum_{j\in\partial_i} w_{ij} \log\left(K_j^{trans}\right),\ 1/\sum_{j\in\partial_i} w_{ij}\right)$$

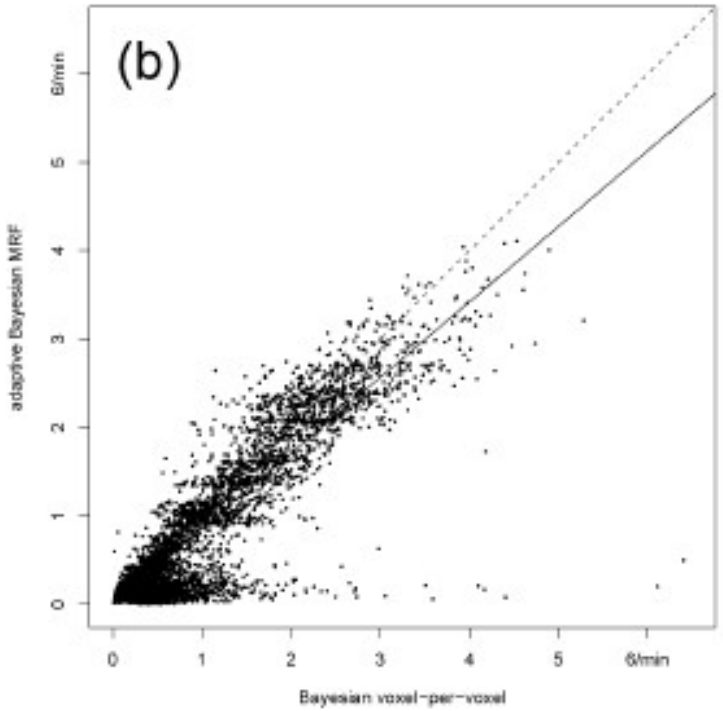
- Spatial smoothing has to account for edges and sharp features
- Smoothing weights w_{ij} are estimated locally and adaptively from the data

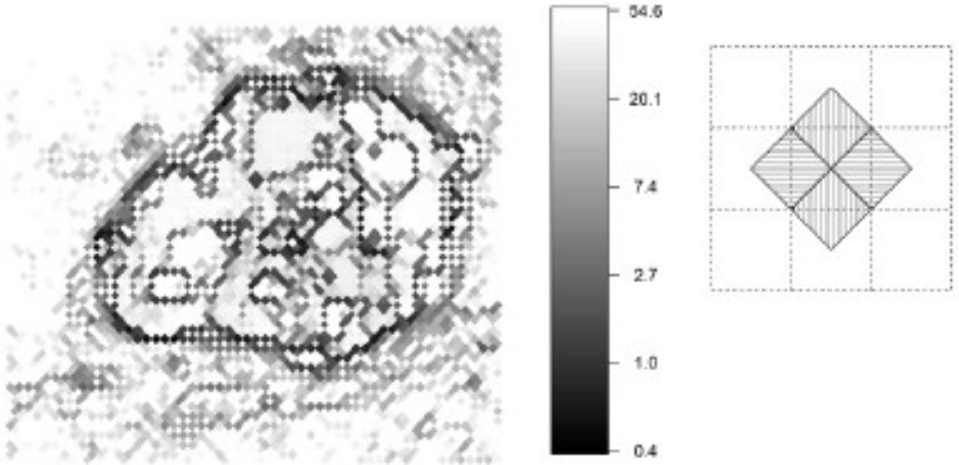
Results spatial DCE-MRI



Schmid, Whitcher, Padhani, Taylor, Yang, IEEE TMI (2006), 25:12, 1627-1636

Results spatial DCE-MRI





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Longitudinal drug studies

- In longitudinal drug studies, we are interested in finding differences in the 4D images
- For example, anti-angiogeneis drugs should lower K^{trans} values
- Standard procedure:
  - Estimate K^{trans}
  - Compute average K^{trans} per scan
  - Test on differences between groups
- Low patient numbers
- Information loss by averaging

Patient ID	Pre	post
1	0.208	0.161
2	0.355	0.120
3	0.255	0.031
4	0.230	0.245
5	0.199	0.208
6	0.154	0.173
7	0.264	0.327
8	0.198	0.223
9	0.305	0.122
10	0.267	0.221
11	0.432	0.111
12	0.174	0.113

Contextual information for Longitudinal Studies

Voxels are from a scan

Scans are from a patient

Patient has some response to treatment and has certain properties (covariates *z*)

→ Use mixed effect model as contextual information

$$\log(K_{is}^{trans}) = \alpha^T z + \beta x_s + \gamma_i + \delta_i x_s + \varepsilon_{is}$$

α, β fixed effects; γ, δ, ε random effects

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LoMIS
Longitudinal Medical Imaging Studies

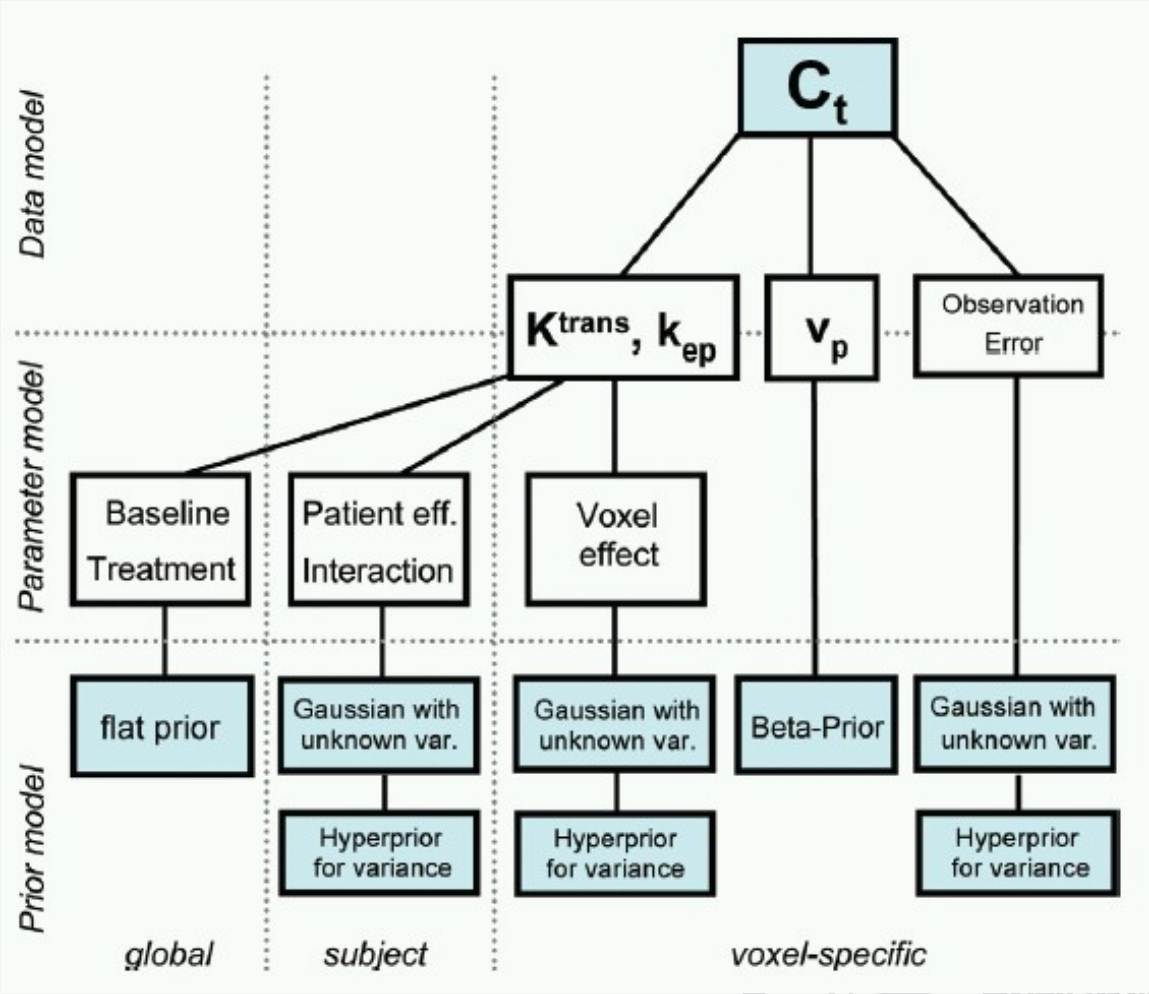
Observed data

Local kinetic model

Context

(study model)

Prior information



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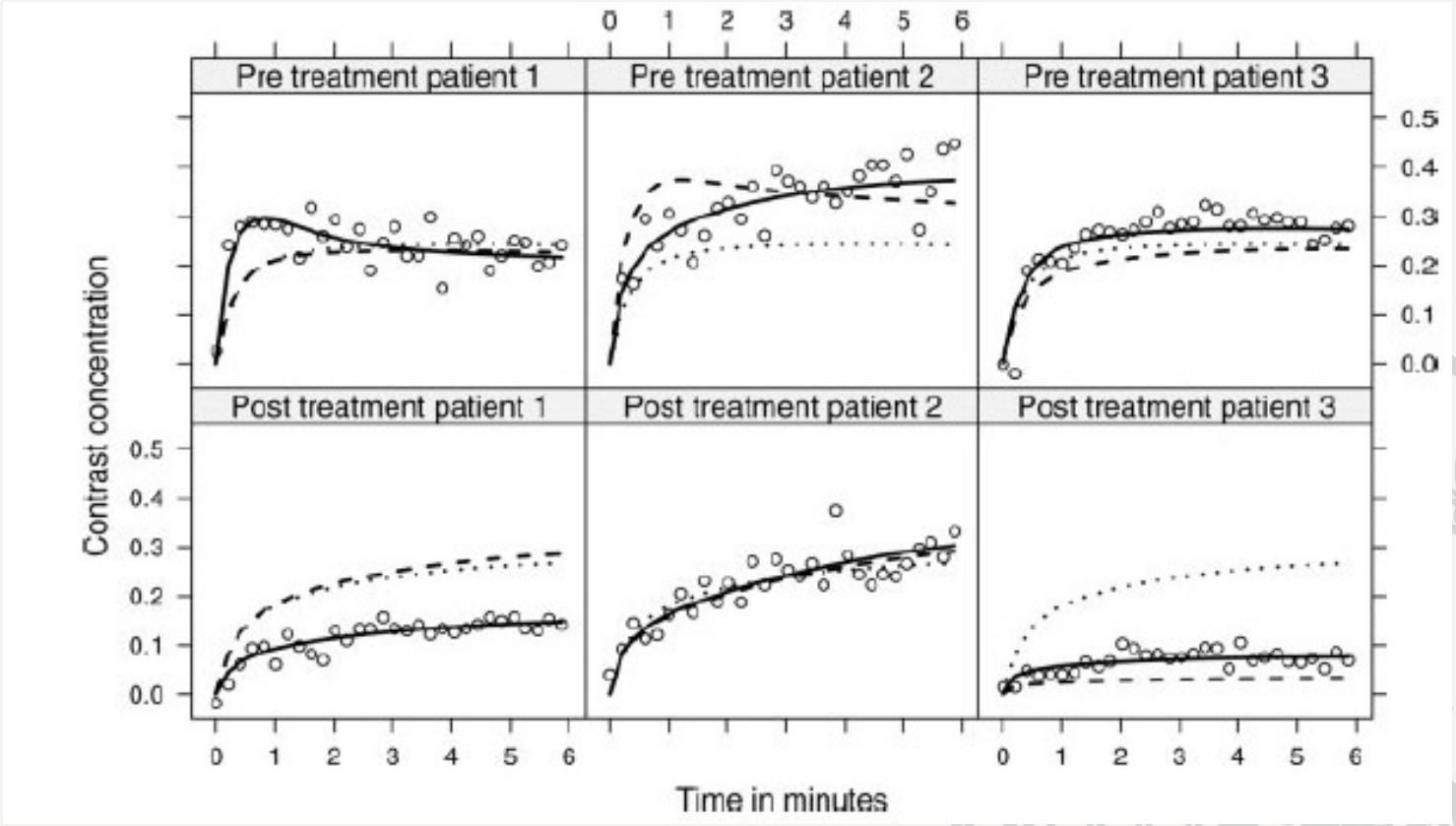
Mixed effect time curves



Schmid, Whitcher, Padhani, Taylor, Yang, MRM (2009), 61, 163-174

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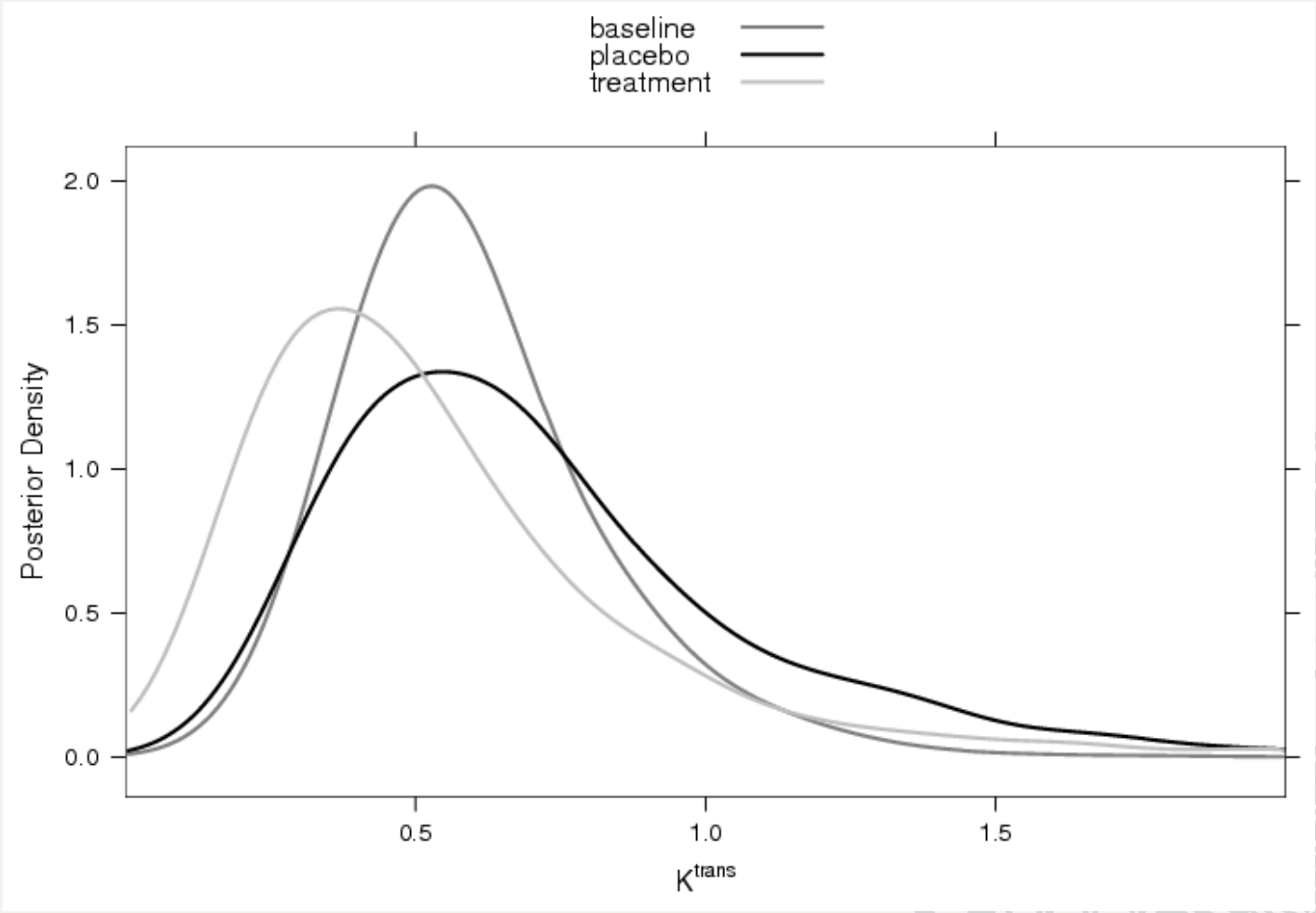
Results LoMIS



Whitcher, Schmid *et al*., Magn.Res.Mat. 24:2 (2011)

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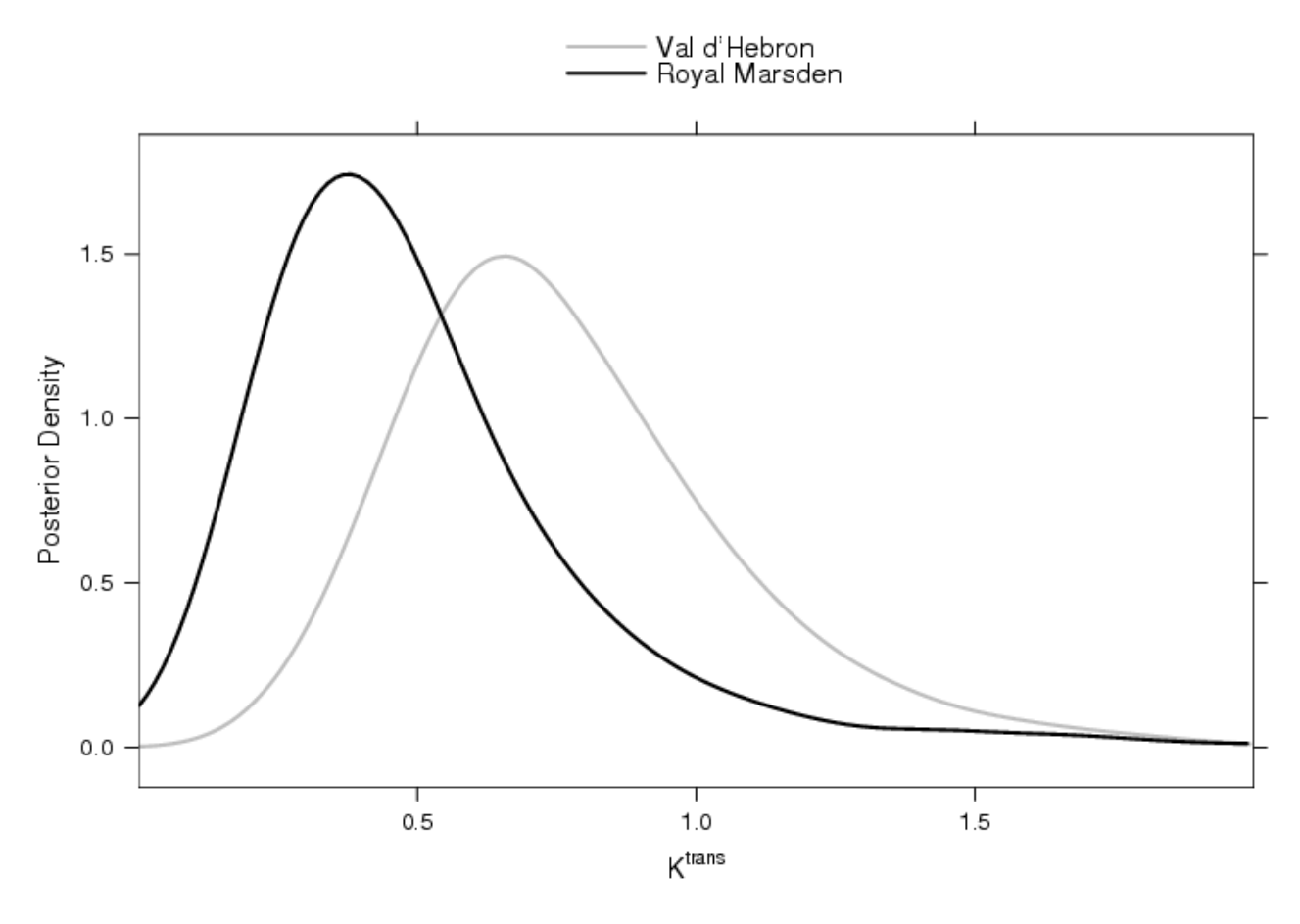
Results LoMIS



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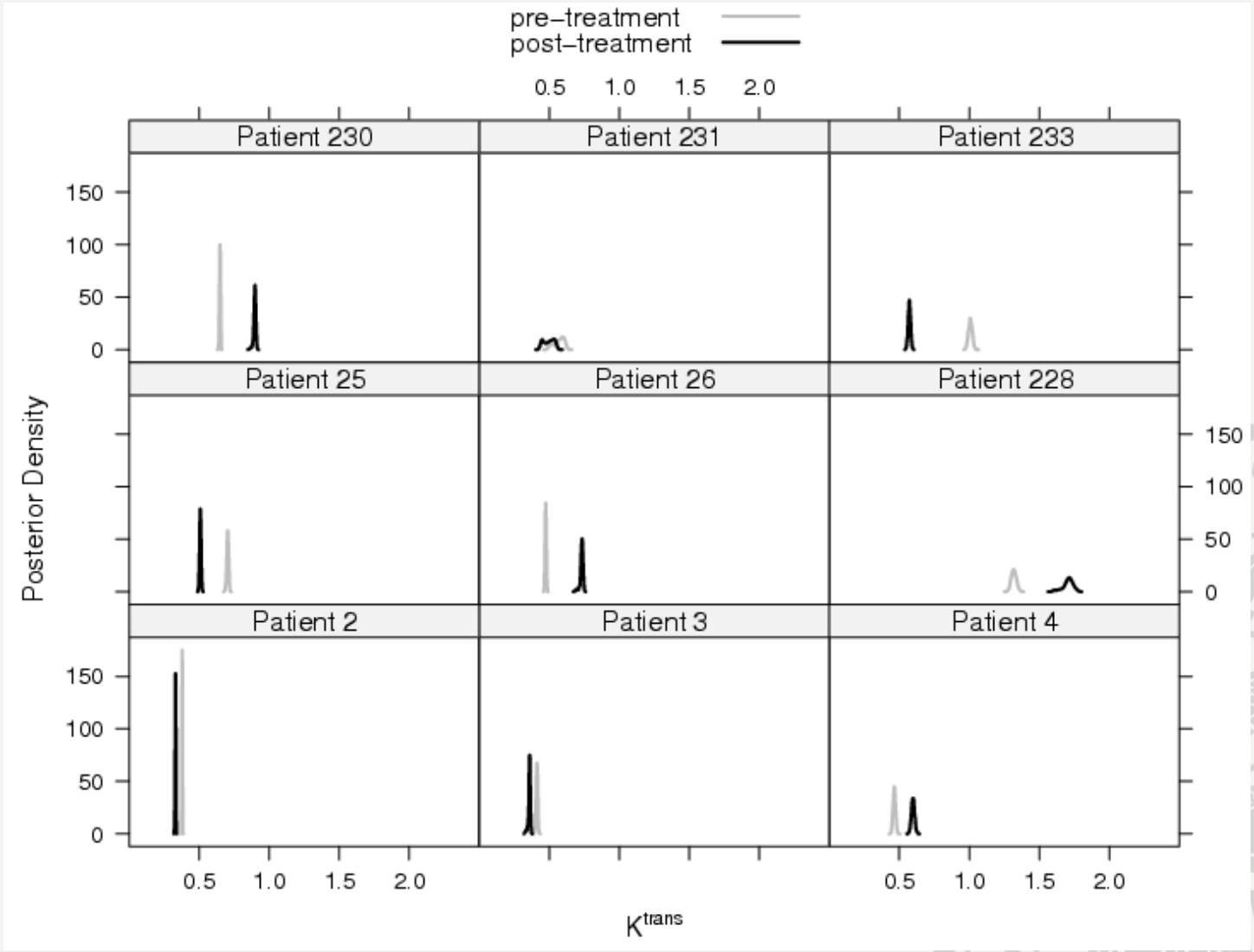
Results LoMIS



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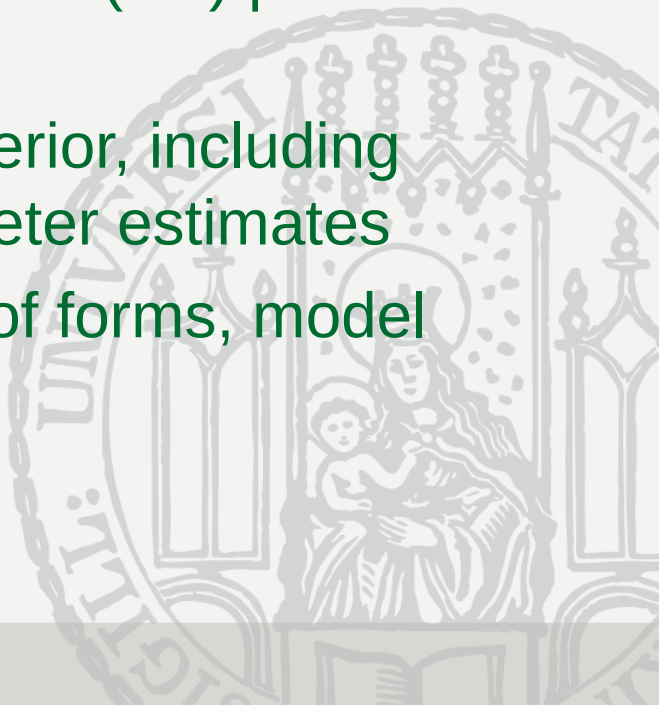
Conclusions

- We use contextual information to
  - Gain strength for local model fitting
  - Gain information on dependencies (allows tests)
- Contextual information is defined via (flat) prior distributions
- Conclusions are drawn from posterior, including uncertainty information on parameter estimates
- Local models can have a variety of forms, model choice (?)



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